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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,831	08/30/2001	Reinhard Ebner	PT049P1	8237

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,831	EBNER ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13 and 23-42* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). ____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: Alignment

DETAILED ACTION

Status of the Application

Claims 12-13, 23-42 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's cancellation of claims 1-11, 14-22, addition of claims 23-42, and election with traverse of Group I, claims 1-10, 14-16 drawn to the polynucleotide of SEQ ID NO: 6 or polynucleotides encoding the polypeptide of SEQ ID NO: 20, vectors, and host cells comprising said polynucleotides, in a communication filed on 11/17/2003, are acknowledged.

Applicant's traverse is on the ground(s) that with respect to a given sequence, a search of the claims of the groups directed to that sequence would also provide useful information for the claims of other groups directed to that sequence. Applicants submit that publications disclosing proteins would also provide information regarding nucleic acids encoding the protein, antibodies to the proteins, and methods of making and using them. As such, it is Applicant's contention that a search of all Groups I-VIII would not impose an undue burden on the Office.

While it is true that publications containing protein information may disclose the nucleic acid encoding such protein and possibly antibodies specific to such protein, it is false to assume that the only source of information about a polynucleotide or an antibody is one in which information about the protein encoded by it is disclosed. Furthermore, publications disclosing protein information may not provide any information as to methods of use of the protein, let alone methods of use of the polynucleotide. Therefore, examination of all the groups would require not only searching for polypeptide information but it would also require searching information regarding the polynucleotide and the claimed methods of use, as well as antibody information. It is also noted that a comprehensive examination of all the inventions would require sequence, patented and non-patented literature, and class/subclass searches which may not

be coextensive. As such, examination of all the inventions would impose an undue burden on the Office.

The requirement is deemed proper and therefore is made FINAL.

Claims 13-14 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. While the elected claims have been canceled, newly added claims 23-42 are directed to the elected invention and will be examined as follows.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/186,350 filed on 03/02/2000.

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to PCT/US01/06256 filed on 02/28/2001.

Claim Objections

3. Claim 33 is objected to due to the recitation of "polynucleotide .....cDNA clone". For clarity, it is suggested that the term "clone" be deleted since this term is associated with cells and the claim is making reference to polynucleotides. Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 23-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

Claims 23-42 are directed to (1) polynucleotides comprising the polynucleotide of SEQ ID NO: 6 or encoding the polypeptide of SEQ ID NO: 20, (2) polynucleotides comprising the cDNA contained in plasmid HIBCJ89, (3) vectors comprising the polynucleotides of (1) or (2), (4) host cells comprising the polynucleotides of (1) or (2), and (5) methods of producing the polypeptides encoded by the claimed polynucleotides.

The specification in page 35 discloses that the polynucleotide of SEQ ID NO: 6 encodes the polypeptide of SEQ ID NO: 20 and corresponds to Gene No. 5 (first entry of Table in page 35). The specification indicates that the polypeptide corresponding to Gene No. 5 (SEQ ID NO: 20) has homology to members of the serine/threonine family of phosphatases and concludes that the polypeptide of SEQ ID NO: 20 is expected to share some biological activities with members of the serine/threonine family of phosphatases (page 18, paragraph 63). According to the specification, since the polynucleotide of SEQ ID NO: 6 was found in CNS (Central Nervous System) tissues, the polynucleotides and polypeptides of the instant invention are useful for the diagnosis, prognosis, prevention and/or treatment of diseases and/or disorders of the CNS. Furthermore, the specification indicates that the polynucleotides/polypeptides of the instant invention may also play a role in the treatment and/or detection of developmental disorders associated with developing embryo or sexually-linked disorders (page 19, paragraph 67).

While the specification suggests that the polypeptide of SEQ ID NO: 20 may share some biological activities with serine/threonine phosphates, and indicates that the polynucleotides/polypeptides of the instant invention can be used for diagnosis, prognosis, prevention and/or treatment of diseases or disorders of the CNS as well as for treatment and/or detection of developmental disorders or sexually-linked disorders, the claimed invention does not meet the utility requirements for the following reasons.

There is no experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having serine/threonine phosphatase activities. The suggested function for the

claimed polynucleotides has been determined solely on the basis of structural similarity (i.e. sequence homology) to a human phosphatase disclosed in WO 97/350015 by Poustka et al. (U.S. Patent No. 6,312,688), as indicated in paragraph 63, page 18. The state of the art clearly teaches the unpredictability of assigning function based on sequence homology and acknowledges that small changes can drastically change function. Bork (Genome Research, 10:398-400, 2000) teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of known error margins for high-throughput computational methods. Bork also indicates that one of the causes of this inaccuracy is that the quality of data available is still insufficient, especially data relating to protein function. Furthermore, Bork teaches that protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Examples of pitfalls associated with comparative sequence analysis for predicting function are shown by Broun et al. (Science 282:1315-1317, 1998), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Witkowski et al. (Biochemistry 38:11643-11650, 1999). Van de Loo et al. teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Broun et al. teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Witkowski et al. teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different biological function.

The polypeptide of SEQ ID NO: 20 shares at best 11.3% overall sequence homology with the tyrosine phosphatase of Poustka et al. (SEQ ID NO: 2) and the polynucleotide of SEQ ID NO: 6 shares at best 3.6% overall sequence homology with the polynucleotide encoding the polypeptide of Poustka et al. (SEQ ID NO: 1). See attached alignments. It is noted that the polypeptide of Poustka et al. is a tyrosine

phosphatase whereas the specification teaches that the polypeptide of SEQ ID NO: 20 shares biological activities with serine/threonine phosphatases. In addition, the specification is silent in regard to the critical structural elements in the polynucleotide of SEQ ID NO: 6 or the polypeptide of SEQ ID NO: 20 which are indicative of serine/threonine phosphatase activity. In view of the unpredictability of annotating function based on sequence homology, as evidenced by the teachings of Bork, Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al. as well as the low % sequence homology between the polynucleotides/polypeptide of the instant application and the closest homologs indicated in the specification, one of skill in the art cannot reasonably conclude that the suggested function for the polypeptide encoded by the claimed polynucleotides is that of a serine/threonine phosphatase or even a tyrosine phosphatase absent additional supporting evidence such as an indication of which are the critical structural elements present in the claimed polynucleotides which are characteristic of other polynucleotides encoding serine/threonine phosphatases or even experimental evidence of the suggested biological function. In the instant case, the specification fails to provide any information or experimental evidence which would support Applicant's suggested biological function, other than the disclosure of the closest structural homologs.

In addition, it is noted that even if one assumes that the suggested function for the polypeptide encoded by the claimed polynucleotides is that of a serine/threonine phosphatase, the specification fails to disclose sufficient information to conclude that there is a substantial and specific utility associated with the serine/threonine phosphatase polynucleotide/polypeptide of the instant invention. The specification fails to provide any clue as to which are the specific biological activities shared with serine/threonine phosphatases and the polypeptide of SEQ ID NO: 20. There is no information as to which is the target of the polypeptide of SEQ ID NO: 20 (i.e. substrate), its specificity, the biological pathway where this polypeptide is active, or its biological role. Furthermore, there is no information as to whether the expression of the claimed polynucleotides, or lack thereof, is indicative of disease. In addition, it is noted

that while the specification provides a long list of several CNS disorders (paragraph 67), there is no teaching as to how one can determine which one of the diseases listed is associated with a particular individual or which are the expression levels associated with each of the diseases listed. No information has been provided as to which developmental disorders or sexually-linked disorders are associated with the claimed polynucleotides and which expression levels are indicative of disease.

As known in the art and indicated by the specification (Background of the Invention), serine/threonine phosphatases are a family of proteins which play critical roles in a wide range of biological activities. Therefore, one would expect a serine/threonine phosphatase to be rather specific in regard to its target substrates and function. Since the substrates, the cellular function of the suggested serine/threonine phosphatase of SEQ ID NO: 20 and the biological processes associated with the polypeptide of SEQ ID NO: 20 and its substrates are all unknown, the utilities recited in the specification are not specific. These utilities are also not substantial since they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is required to study the properties of the claimed polynucleotides and the corresponding polypeptide as well as the mechanisms in which the claimed polynucleotides are involved. Since the instant specification does not disclose an specific and substantial "real world" use for the polynucleotide of SEQ ID NO: 6 or a polynucleotide encoding the polypeptide of SEQ ID NO: 20, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

6. Claims 23-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established

utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

7. No claim is in condition for allowance.

8. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
January 7, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600